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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/527,772

04/18/2005

Kenji Tanaka

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EXAMINER

STEELE, AMBER D

ART UNIT

PAPER NUMBER

1639

MAIL DATE

DELIVERY MODE

06/17/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/527,772	Applicant(s) TANAKA ET AL.	
	Examiner AMBER D. STEELE	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 April 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,6 and 8-14 is/are pending in the application.
- 4a) Of the above claim(s) 1-4,6,12 and 13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8-11 and 14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 March 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Status of the Claims

1. The amendment received on November 9, 2007 amended claims 1 and 8, canceled claim 5, and added new claims 12-13.

The amendment received on April 20, 2009 amended claims 1 and 8-10, canceled claim 7, and added new claim 14.

Claims 1-4, 6, and 8-14 are currently pending.

Claims 8-11 and 14 are currently under consideration.

Election/Restrictions

2. Applicants elected, with traverse, Group II (previous claims 8-11) in the reply filed on November 9, 2007. Claims 1-4, 6, and 12-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Potential Rejoinder

3. Applicants elected claims directed to the product, if a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

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In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all the criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained.

Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See “Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b),” 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to a rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Priority

4. The present application claims status as a National Stage application (i.e. 371) of PCT/JP04/10540 which is a CIP of 10/622,002 filed July 17, 2003.

5. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-

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filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 10/622,002, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. U.S. application 10/622,002 does not provide support for a weight ratio of membrane proteins to lipids from 0.01 to 0.8 (i.e. 0.05 or less was found), a lower limit of 10^5 regarding library members (i.e. 10^6 is lowest limit), or the open-ended range of 10 nm or more regarding the diameter of the liposomes. Therefore, the presently claimed invention has a priority date of the filing date of PCT/JP04/10540 (filed July 16, 2004).

Declaration

6. The declaration under 37 CFR 1.132 filed April 20, 2009 is insufficient to overcome the rejection of claim 14 based upon 35 USC 103 (a) as set forth in the last Office action because: Tanaka et al. WO 02/056026 published July 18, 2002 (effective filing date of January 9, 2001) is considered art under 35 USC 102(a) and 102(b) due to the lack of priority to U.S. application 10/622,002 (i.e. 10 nm or more).

Invention as Claimed

7. Independent claim 8: A library of membrane protein-embedded liposomes comprising about 1×10^5 or more membrane protein-embedded liposomes which is obtained by (a) providing a library of membrane proteins and (b) contacting the library of membrane proteins with liposomes to form a library of membrane protein-embedded liposomes wherein the weight ratio of the membrane proteins to lipids constituting the liposomes is from 0.01 to 0.8 wherein the

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liposomes have a diameter of 10 nm or more and wherein the amount of membrane proteins per library is about 10 fg or more and variations thereof.

8. Independent claim 14: A library of membrane protein-embedded liposomes comprising about 1×10^6 or more membrane protein-embedded liposomes which is obtained by (a) providing a library of membrane proteins and (b) contacting the library of membrane proteins with liposomes to form a library of membrane protein-embedded liposomes wherein the weight ratio of the membrane proteins to lipids constituting the liposomes is form 0.05 or less wherein the liposomes have a diameter of 10 nm or more and wherein the amount of membrane proteins per library is about 10 fg or more and variations thereof.

9. The presently claimed product contains process limitations which are considered product-by-process limitations. See MPEP § 2113. Only the structural limitations will be provided patentable weight.

Withdrawn Objections

10. The objection to claims 8-11 is withdrawn in view of the claim amendments received on April 20, 2009.

Withdrawn Rejections

11. The rejection of claims 8-11 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the claim amendments received on April 20, 2009.

Maintained Rejections

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 8-11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Allen et al. U.S. Patent 6,056,973 issued May 2, 2000 and Tanaka et al. WO 02/056026 published July 18, 2002 (effective filing date of January 9, 2001).

For present claims 8-11 and 14, Allen et al. claim a library of liposomes (e.g. library = more than one; open-ended range encompassing 10^5 , 10^8) comprising proteins including antibodies, Fab, ICAM-1, VCAM-1, etc. wherein the liposomes are 100 nm in diameter, between 1-20 mole percent of lipid is present in the liposome formation, 1.2 mole percent of protein, and 12, 20, 33, 40, and 70 proteins can be in each liposome wherein the proteins can have molecular weights of 3,000 Da (Fab), 90-110 kDa (ICAM-1), etc. (please refer to the entire specification particularly columns 2-8).

However, Allen et al. does not specifically teach 10 fg, 1 pg, 10 pg, or more protein.

For present claims 8-11 and 14, Tanaka et al. teach protein embedded liposomes comprising ng amounts of protein (please refer to the entire specification particularly Figure 19; Examples 1-5).

The claims would have been obvious because the substitution of one known element (i.e. liposome with less than 10 fg, 1 pg, or 10 pg protein as taught by Allen et al.) for another (i.e.

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liposome with ng amount of protein taught by Tanaka et al.) would have yielded predictable results (i.e. more protein in liposome) to one of ordinary skill in the art at the time of the invention. In addition, if “a person of ordinary skill has good reason to pursue the known options within his or her technical grasp” (e.g. size of library, size of liposome, etc.), then “it is likely the product is not of innovation but of ordinary skill and common sense”. Furthermore, it is noted that various limitations including the size of the library, the size of the liposome, the weight ratio, and the amount of protein are normal experimental design choices and/or optimization for a desired outcome and routine in the art. As evidenced by Munechika et al. U.S. Patent 5,662,931 issued September 2, 1997, the prior art teaches various potential weight ratios including protein to lipid ratio of 0.1 to 0.5 and 0.01 to 10 parts by weight (please refer to the entire specification particularly column 3, lines 1-24; see also the abstract; columns 2-3) that could be utilized for liposome libraries. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Arguments and Response

14. Applicants’ arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Allen et al. and Tanaka et al. for claims 8-11 and 14 were considered but are not persuasive for the following reasons.

Applicants contend that Allen et al. teach liposomes greater than 10 nm in diameter (e.g. 100 nm). Applicants also contend that Allen et al. does not teach a weight ratio of 0.01 to 0.8 or 0.05 or less.

Applicants’ arguments are not convincing since the teachings of Allen et al. and Tanaka et al. render the libraries of the instant claims *prima facie* obvious. The present claims (independent claims 8 and 14) require the liposomes to have a diameter of 10 nm or more

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(emphasis added). Allen et al. teach liposomes of 0.01 to 0.5 micron, 0.03 to 0.4 micron, 100 nm or less, 105 nm, 99 nm, 98 nm, etc. (please refer to the entire specification particularly column 10, lines 35-53; column 13, lines 22-29; Table 2; Example 1). See MPEP § 2144.05.

Regarding applicants assumed molecular weight of lipid constituting a liposome is about 800 and the average molecular weight of membrane proteins typically is several tens of thousands of Daltons (e.g. 30 kDa) to determine that Allen et al. teaches a weight ratio of about 2 to about 40 or more, the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) (“An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.”).

Furthermore, it is noted that various limitations including the size of the library, the size of the liposome, the weight ratio, and the amount of protein are normal experimental design choices and/or optimization for a desired outcome and routine in the art. As evidenced by Munechika et al. U.S. Patent 5,662,931 issued September 2, 1997, the prior art teaches various potential weight ratios including protein to lipid ratio of 0.1 to 0.5 and 0.01 to 10 parts by weight (please refer to the entire specification particularly column 3, lines 1-24; see also the abstract; columns 2-3) that could be utilized for liposome libraries. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007). See MPEP § 2144.05. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to

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discover the optimum or workable ranges by routine experimentation.” In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In addition, it is noted that Allen et al. teach that the liposome can have between 1-20 mole percent of derivatized lipid, the rest of the lipids are vesicle-forming lipids, liposomes with 12, 20, 33, 40, and 70 Fab with molecular weights of 3,000 daltons (i.e. 10-fold less than what applicants utilized for their calculation), 1.2 mole percent of targeting conjugates (i.e. derivatized lipid to protein ratio of 0.06 which excludes the additional vesicle-forming lipids; please refer to the entire specification particularly columns 8-10 and 14; Examples 1-2).

15. Claims 8-11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perrott et al. U.S. Patent 6,217,901 issued April 17, 2001; Tanaka et al. WO 02/056026 published July 18, 2002 (effective filing date of January 9, 2001); and Munechika et al. U.S. Patent 5,662,931 issued September 2, 1997.

For present claims 8-11 and 14, Perrott et al. teach synthetic polymer complements (SPCs; liposomes; plurality = library, open-ended range of two or more encompassing 10^5 , 10^8) that range in size from about 20 to about 1000 nm and containing 1 to about 10,000 template molecules which can be membrane proteins (please refer to the entire specification particularly the abstract; Figures 1A-1C; columns 2-4, 9-11).

However, Perrott et al. does not teach 10 fg, 1 pg, or 10 pg of protein.

For present claims 8-11 and 14, Tanaka et al. teach protein embedded liposomes comprising ng amounts of protein (please refer to the entire specification particularly Figure 19; Examples 1-5).

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However, Perrott et al. does not teach weight ratio of proteins to lipids of 0.01 to 0.8.

For present claims 8-11 and 14, Munechika et al. teaches liposomes containing physiologically active proteins at a protein to lipid ratio of 0.1 to 0.5 and 0.01 to 10 parts by weight (please refer to the entire specification particularly column 3, lines 1-24; see also the abstract; columns 2-3).

The claims would have been obvious because the substitution of one known element (i.e. liposome with less than 10 fg, 1 pg, or 10 pg protein as taught by Perrott et al.; liposome with unknown weight ratio as taught by Perrot et al.) for another (i.e. liposome with ng amount of protein taught by Tanaka et al.; weight ratio of 0.1 to 0.5 taught by Munechika et al.) would have yielded predictable results (i.e. more protein in liposome; specific protein to lipid ratio) to one of ordinary skill in the art at the time of the invention. In addition, if “a person of ordinary skill has good reason to pursue the known options within his or her technical grasp” (e.g. size of library, size of liposome, etc.), then “it is likely the product is not of innovation but of ordinary skill and common sense”. Furthermore, it is noted that various limitations including the size of the library, the size of the liposome, the weight ratio, and the amount of protein are normal experimental design choices and/or optimization for a desired outcome and routine in the art. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Arguments and Response

16. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Perrott et al., Tanaka et al., and Munechika et al. for claims 8-11 and 14 were considered but are not persuasive for the following reasons.

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Applicants contend that Perrott et al. liposomes that range in size from 20-1000 nm. Applicants contend that one of ordinary skill in the art would not have had any reason to combine the disclosure of Munechika et al. with the disclosures of Perrott et al. and Tanaka et al. because Munechika et al. teach water-soluble proteins while Perrott et al. and Tanaka et al. teach membrane proteins.

Applicants' arguments are not convincing since the teachings of Perrott et al., Tanaka et al., and Munechika et al. render the libraries of the instant claims *prima facie* obvious. The present claims (independent claims 8 and 14) require the liposomes to have a diameter of 10 nm or more (emphasis added). Perrott et al. teach liposomes of 20 to 1000 nm (please refer to the entire specification particularly the abstract; column 4, lines 30-40).

Munchika et al. teach various proteins that can be part of a liposome library including M-CSF which has a membrane bound form (see column 2, lines 8-26; reference will be provided upon request).

Furthermore, it is noted that various limitations including the size of the library, the size of the liposome, the weight ratio, and the amount of protein are normal experimental design choices and/or optimization for a desired outcome and routine in the art. As evidenced by Munechika et al. U.S. Patent 5,662,931 issued September 2, 1997, the prior art teaches various potential weight ratios including protein to lipid ratio of 0.1 to 0.5 and 0.01 to 10 parts by weight (please refer to the entire specification particularly column 3, lines 1-24; see also the abstract; columns 2-3) that could be utilized for liposome libraries. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007). See MPEP § 2144.05. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by

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the prior art unless there is evidence indicating such concentration or temperature is critical.

“[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Conclusion

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Primary Examiner, Art Unit 1639

June 15, 2009